Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Claims 2–5, 162–165, and 173–176 have been cancelled without prejudice, claims 1, 6, 9, 10, 11, 145, 148, 149, 150, 153, 155, 159, 166, 168, 177, 178, 181, 182, 183, and 185 have been amended, and new claims 186-189 have been introduced. No new matter has been introduced by these amendments. Claims 1, 6–11, 13–16, 145–161, 166–172, 177–183, and 185–189 are pending, with claims 145–161, 166–172, 177–180, and 186–188 standing withdrawn. The subject matter of claims 1, 6–11, 13–16, 181–183, 185, and 189 is currently being examined.

This application now contains 3 independent claims and 47 total claims. No excess claim fees are due with this submission.

The objection to claims 181–183 as being directed to non-elected species is respectfully traversed in view of the above amendments.

The rejection of claims 1–11, 13–16, and 185 for obviousness-type double patenting over claim 1 of U.S. Patent No. 6,673,901 to Koide ("Koide I") in view of U.S. Patent No. 6,818,418 to Lipovsek et al. ("Lipovsek") is respectfully traversed. The position of the United States Patent and Trademark Office ("PTO") is, essentially, that the polypeptide monobodies of the present invention would have been obvious from the claimed monobodies of Koide I, because they share a genus–species relationship. Applicants respectfully disagree, because claim 1 of Koide I does not teach or suggest polypeptide monobodies that exhibit estrogen receptor binding activity, as required by the present claims. Accordingly, the rejection of claims 1–11, 13–16, and 185 for obviousness-type double patenting over claim 1 of Koide I is improper and should be withdrawn.

The rejection of claims 1–11, 13–16, 181–183, and 185 under 35 U.S.C. § 112 (2nd para.) for indefiniteness is respectfully traversed. As amended herein, the claims clearly identify the loop region sequences and the N-terminal and C-terminal regions, and what modifications may be made to these portions of the monobody. Further, one of skill in the art would have understood what is meant by the term "derived from the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 3" in the context of the present claims, because the type of modification relative to a corresponding loop region present in SEQ ID NO: 2 or 3 is recited

in each of claims 1 and 185. Accordingly, the rejection of claims 1–11, 13–16, 181–183, and 185 for indefiniteness is improper and should be withdrawn.

The rejection of claims 1–11, 13–16, 181–183, and 185 under 35 U.S.C. § 112 (1st para.) for lack of enablement is respectfully traversed.

The PTO's position is that the present application is only enabling for monobodies with a modified AB, BC, or FG loop. Applicants respectfully disagree. In particular, the β strand sequences of FNfn10 (and the polypeptide monobodies of the present invention) provide a rigid, internal framework for the functional, flexible loop region sequences. The present application demonstrates that monobodies can be made to bind with estrogen receptors by introducing an estrogen receptor-binding sequence into a loop region sequence. Although these monobodies were made with modifications to AB, BC, or FG loop, other loops of FNfn10 polypeptide monobodies can tolerate extensive mutations, including an insertion of amino acid residues, as shown in Batori et al., "Exploring the Potential of the Monobody Scaffold: Effects of Loop Elongation on the Stability of a Fibronectin Type III Domain," *Protein Eng.* 15:1015–20 (2002) (filed with December 2006 submission), which demonstrates that the AB, BC, CD, DE, and FG loops were all shown to be amenable to modification while retaining the stability of the β-strand scaffold. This certainly confirms that estrogen receptor-binding sequences can be grafted into the other loop region sequences of FNfn10 without a detrimental effect on the structural integrity of the FNfn10 scaffold, and that the resulting monobody will exhibit estrogen receptor binding activity. Further, one of ordinary skill in the art would have known how to make modified loop region sequences using standard techniques for protein mutagenesis. Exemplary techniques are described in the present application at page 15, line 14, through page 15, line 24.

The PTO has also taken the position that the present application does not teach what modifications would result in a monobody that has estrogen receptor binding activity. Applicants respectfully disagree, because the present application has ample support for modifications that result in estrogen receptor binding. Indeed, the examples identify approximately fifty (50) species that possess estrogen receptor binding properties (see species recited in claims 181, 182, 183, 186, 187, and 188).

For all of these reasons, the rejection of claims 1–11, 13–16, 181–183, and 185 for lack of enablement is improper and should be withdrawn.

The rejection of claims 1–11, 13, 14, and 185 under 35 U.S.C. § 102(e) for anticipation by Lipovsek is respectfully traversed. Lipovsek relates to proteins that include a fibronectin type III domain having at least one randomized loop. However, Lipovsek does not disclose polypeptide monobodies that exhibit estrogen receptor binding activity, as required by the present claims. Accordingly, the rejection of claims 1–11, 13, 14, and 185 for anticipation by Lipovsek is improper and should be withdrawn.

The rejection of claims 1–11, 13–15, and 185 under 35 U.S.C. § 103(a) for obviousness over International Patent Application No. WO 98/56915 to Koide (Koide II) in view of Lipovsek is respectfully traversed. Koide II discloses various polypeptide monobodies derived from the 10th Fn3 domain of fibronectin. Lipovsek is cited for teaching protein variants of the tenth module of human Fn3 designed to bind to a specific binding partner, including hormone receptors. The PTO has taken the position that one of skill in the art would have recognized that the hormone receptors of Lipovsek include nuclear receptors, and would have anticipated that polypeptide monobodies that bind to nuclear receptors could be made using the directed evolution approach disclosed in Koide II. Applicants respectfully disagree, because Koide II and Lipovsek (alone or in combination) do not teach or suggest polypeptide monobodies that exhibit estrogen receptor binding activity, as required by the present claims. Accordingly, the rejection of claims 1–11, 13–15, and 185 for obviousness over Koide II and Lipovsek is improper and should be withdrawn.

In view of all of the foregoing, applicant submits that this case is in condition for allowance and such allowance is earnestly solicited.

If any fees are due with this submission, the PTO is hereby authorized to charge any fee deficiency to Deposit Acct. 14-1138.

Respectfully submitted,

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